

Does Scientific Progress Come from Projects or People?

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When Bob Clodius called me about speaking today, I of course recalled our good times together at the University of Wisconsin over 30 years ago. I wondered, having worked exclusively at private (a euphemism for federal) research institutions, namely, Stanford and The Rockefeller, all that time, how pertinent my experience would be for you. Of course, we both agreed: all the more reason for discourse, and in any event there is much more that joins private and state institutions in carrying out their research functions than divides them.

Institutions, how they are taken for granted and how they serve as homes for intellect, will be the focus of my discussion. Bob and I and all of us have been giving a lot of thought to their status today. My own experience, and especially my present role, does constrain me to speak most about the research mission—and the academic career of research in the natural sciences.

I won't be saying very much about overall budget priorities—how much we should collect in taxes; how much we should spend for defense, for health, for education. These questions are easy only for the one who doesn't have to make the final decisions about all of these responsibilities of government. So I should not comment on them without giving the same attention to the dilemmas of each sector as I will to my main topic.

Should we be complaining? In terms relative to other countries, or much of our past history, we have a robust scientific enterprise. Yet I believe that, with available funds, we could be far more effective and could get better perspectives on fundamental priority allocations. And trouble is looming in industrial competitiveness and in the morale of younger scientists as they face the problematical attractions of the scientific career. The morale of presidents is of less

broad public concern: Steve Muller asks, Where are the giants of yesteryear? I paraphrase his answer: They are collecting return-deposit beer cans to help pay the bills.

My subject does not lend itself to the scientific process of analysis and verification with which I am most familiar. I will call more anecdotally on 35 years at the laboratory bench and another decade in academic administration for an avowedly subjective appraisal of how federal agency funding, our institutions, and the careers of individual scientists interact in that heady twentieth-century environment for research. The institutions' perspectives will also be noted and also the interaction of these with the incentives and opportunities for unconventional and interdisciplinary initiatives. The skeleton of my remarks comes from a working paper I submitted during my membership on the Packard-Bromley White House Science Council panel on the Health of the Universities. Despite notable deficiencies in that report—it failed to include my paper verbatim—I commend it to you as a high point of examination and mutual understanding of the basic issues of the federal-university relationship today. Predictably, and just as we feared, it is being implemented in a quite selective and lopsided fashion: namely, whatever will save the federal budget short-run dollars. It does give a particularly good account of our problems in compensating for long deferred maintenance and renewal of capital facilities and instrumentation, so I will comment mainly on the issues of operating support for research programs at academic institutions.

1. The investigator's relationship to his/her institution and to the federal grant system.

At the present time, federal funding accounts for a lion's share of the support of



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scientific research at "private" universities and increasingly at state institutions as well. From the perspective of the individual investigator, the dependency on federal funds is even greater, since the nonfederal input will be concentrated on faculty salaries and the institutional infrastructure [which is only partly paid for by indirect cost recovery]. For most investigators at universities, very limited funds for the actual conduct of research are available except from federal sources. Even a momentary interruption of support (while it may not immediately impact the investigator's tenure as a professor) poses grave stresses on the continuity of the research, on the employment of technical staff, and on the capacity and opportunity of the investigator to continue a research career.

Since World War II, the scope of federal support for science has constructively expanded that enterprise to the degree that complaints about the details of research administration, and their qualitative impact, are in some ways ungracious. So long as the dependency on federal funds was less than total, private resources could make up for discrepancies that are difficult to rectify in a government bureaucracy responsive to the politics of both the executive and legislative branches. It is not a good answer to reduce

the scope of our science and technology when we have not exhausted the possibilities of constructive reform in the federal-university relationship.

In recent years the overall financial stresses on institutions, coupled with stern policies of federal agencies that limit the institutions' flexibility and draw down their small uncommitted reserves, have left little buffering capacity on the institutions' part to reinsure against contingencies.

The predictable consequence is a confusion of responsibility for the career interest of the scientist: the federal government has the means for financial flexibility but eschews the responsibility; conversely, the institution has the responsibility but not the means. The loyalties of the scientist are likewise divided and confused. Only the most accomplished and fortunate can look beyond the imperative of qualifying for renewal of their research grant. Then pushed aside are all other activities, including intellectual cooperation in education as well as research, risk taking in the planning of research, even reaching out for technology transfer in applying new science. New structural approaches to encouraging interdisciplinary ventures are being actively pressed, especially by the National Science Foundation (NSF); but that top-down approach may even compound the problem if it does not look closely at the dynamics of the careers of the creative individuals who are the real wellspring of science and technology productivity: their functioning before and after, as well as during, their participation in these new structures. In my view the best way to foster interdisciplinary creativity is not to impose new structures, but to liberate individual scientists to reconstellate themselves as called for by the scientific opportunity. (As this is becoming a controversial policy debate, I must display my credentials: my experience in interdisciplinary and applications-oriented work embraces not only molecular biology, but also applied biotechnology, world health, computer science, space exploration, and international relations.) Even existing academic structures have become necessary evils, in some respects,

from the perspective of encouraging novel individual initiatives. They will be aggravated by the cluttering of the organizational landscape with still more crosscutting rigidified "improvements" that then take on a life of their own.

Further compounding these constraints has been the trend in grants administration, during the past decade, ever more to the *project* rather than the investigator as the locus of merit. Short terms of grant awards have enhanced the opportunity and incentive for micromanagement of others' research, even on the part of peer scientists. This sets up another vicious cycle, that the burden of grants review constricts the pace and volume of feedback between the investigator and the review process. It is not unusual for an application for a two-year grant to require a year's lead time, and then—with very short notice—difficulties crop up in the prospects of renewal that would then imperil the continuity of the work.

There is great value in peer review—e.g., the gatekeeping of the refereed journals—which provides indispensable objective criticism and public exposure of new findings and ideas. At present, however, investigators are typically spending 20-30 percent of their time and energy in sustaining the flow of grant support and in a setting of high anxiety that can only interfere with their creative thinking. (Yes, there is some optimal level of accountability and arousal, but no one can justify what is experienced today.)

Widely misunderstood, however, it is not the peer-review but the project system that is the root of this stress, although it is "peer review" that has attracted vocal criticism. Who better than other working scientists could maintain critical oversight on the quality of science? Of course, one's colleagues are also one's competitors, and during times of stringency one needs to take special precautions against interested bias and devices to insist on the accurate reflection of judgments pooled from individual ballots. I have found that demanding a rank-ordering of judgments helps on both counts: to reduce the negative impact of one idiosyncratic vote, which gives undue weight to a single

blackball when all the absolute votes are simply averaged, and to force the judges to express difficult choices, closer to the consequences of their votes. In the end, after all, the proposals will have to be rank-ordered in some way to reach a decision on which will be funded.

Needless to say, the judges should be true peers, scientists of experience and accomplishment—a goal hard to achieve when all have been so exhausted by their prior service: more about that later.

It is the short-term emphasis on projects that amplifies the stresses on individual careers. This is then matched by the systemic waste that flows from intermittent encouragement and distress, the nurturing of careers that are allowed to sprout, followed by intervals of drought or decapitation. The project system leaves all too little latitude for intrainstitutional measures of criticism and support. In a word, careers are being administered, *de facto*, by a distant bureaucracy that accepts little responsibility for this facet of the scientific enterprise, while the system leaves few resources to local communities of scholars to guide the evolution of their scholarship or the reeducation of their (possibly temporary) weakest links. Altogether, the project system is in violent contradiction with the professorial system at the university. We would not cast on the dust-heap a brilliant teacher who had one bad year. But this is precisely the prospect facing the research career today. Still embedded in the project system is the ideology that scientific research is an amateur vocation—a discretionary incidental to teaching—to which the investigator can return after a brief fling. I don't know how else to understand the preoccupation of the NSF with summer salaries as its avenue of support of principal investigators. Perhaps even to a fault—one could argue about that—research is no longer an ancillary function of the university: it is the principal criterion of recruitment to our major universities. I have heard some agencies brag that the average duration of grant support was ~~seven~~ years—that was supposed to be an index that everybody could get a ride on the trolley car. They had

made no enquiry and obviously could know little about what happened after they had been pushed off for the new crowd, nor the waste entailed in that seesaw style.

These frictions first frustrate, then deter many young scientists. I am not aware of other than anecdotal evidence that many gifted students are turning away from scientific careers in anticipation of these problems. The evidence is clear that very few MDs now are willing to embrace the risks of a research career as against the incentives of a specialty practice (and against a background of debt for paying for their MD education that puts them under extreme burden). While most of the emphasis, perhaps correctly, has been placed on the decline of secondary and undergraduate education in science, these motivational factors should not be ignored.

The PhD graduate or MD contemplating research must look forward to a lifelong career of seeking project grants. His most promising years may be those in graduate school and as a postdoctoral fellow when he or she at least has the administrative and financial shelter of an established laboratory. We should not lose sight of the often contradictory demands on the scientific personality: antitheses such as imagination vs. critical rigor, iconoclasm vs. respect for established truth, humility and generosity to colleagues vs. arrogant audacity to nature, efficient specialization vs. broad interest, doing experiments vs. reflection, ambition vs. sharing of ideas and tools—all these and more must be reconciled within the professional persona. They are intrinsic to the nature of science. We should work hard to avoid piling on gratuitous stresses that discourage, even deter, some of the worthiest young people seeking scientific careers today. They are perhaps most clearly telling in the trepidations of well-qualified minorities about entering graduate research and careers in science, compared to the safe course of law, business, or medicine.

2. Remedies.

A far-reaching reconstruction of the federal-university relationship probably exceeds

realistic goals and certainly would require still more extensive deliberation. It appeared to be working admirably from about 1950 to 1965, and, while the high rates of annual increase in appropriations cannot be replicated, some other features perhaps can. This approach has the merit of replicating experiments already done within the corporate memory of granting agencies.

Some essential features include

a. Above all, recognition that an institution's administration is a processing center for flows of resources, not a primary fount. The "partnership" simile (of government and university) is a constructive image, but it may be misleading about the revenue-raising capabilities of the partners.

It is elementary but still must be explained to grantors (public and private) that whatever the grant system does not provide can only be compensated for by

- (i) taking resources away from another activity
- (ii) discovering other sources (unlikely!)
- (iii) shrinking the program

Suggestions that "the institution should pay for" are rarely accompanied by informed mandates as to the sources that should be tapped. Faculty should not be excessively burdened with factual knowledge about administrivia; indeed they are often equally ill-informed about this principle, e.g., in discussions of indirect cost recovery. Complex institutions, like academic medical centers, may need to improve their own cost accounting for their own awareness of the cross-flows, and many questions doubtless can and should be asked about them. This oversight of institutions' policies is not well done by ad hoc demands around single, vulnerable projects on the part of agencies that will not share responsibility for the reconstruction that will be entailed.

b. Restoration of emphasis on the creativity of individual investigators, rather than the substance of a research proposal, as the central criterion of merit. Re-

search is after all a foray into the unknown and unpredictable. The skills needed are, above all, those for improvisation in the face of unexpected discovery or disappointment. Those skills are not evenly distributed, and a carefully thought-out proposal is important testimony about them. That writing cannot, however, substitute for proven and sustained accomplishment and, especially, for research of an exploratory (versus exploitative) character. It is infuriating to see critiques worded like "The investigator has not demonstrated [in advance] that he can [discover such and such]" addressed to individuals who have repeatedly surprised the scientific community (and themselves) with their prior innovations. No wonder that many innovative minds now bootleg their most creative ideas under the cover of "sure-thing" applications or, as a variant, write their proposals around work already completed. And what a waste that their ingenuity should be so expended! The implication that an investigator should "know what he is doing" before being worthy of a grant flies in the face of the actual history of the most creative discovery. How would a project proposal to NSF have fared that looked to explore the high-temperature superconductivity of ceramics? And I will aver in retrospect about my own career since 1946 that none of my own most consequential discoveries had been telegraphed in project proposals beforehand. About the most important matters, we are *always* too ignorant in advance to spell out the discoveries we might make.

3. Lengthening the period of award.

A change of culture, or rather a regression to the 1960s era of the National Institutes of Health and NSF and the 1950s of the Office of Naval Research, will not happen spontaneously nor readily. The bureaucracies of most institutions and agencies have become ever more professionalized,

viz., as professional administrators, and only those rare individuals who have had personal experience of creative scientific research are likely to have the skill and experience to know how to oversee these changes of outlook—a problem especially taxing for the middle, i.e., working, levels of management.

We then have to think of the most effective managerial devices to work these changes without entailing the reeducation of hordes of effector agents. My candidate is one fell swoop of administrative fiat, namely, a mandate that grant awards again be typically for five to seven years. This would reduce the administrative load of reviewing grant proposals, and likewise, on the investigators, especially if there were a period of grace for the more gradual phasedown of a nonrenewable project. Reducing the now intolerable workload of review would conserve the precious resource of competent peers. It might also enable a discourse between applicant and reviewers that is now rigid and full of mutual misunderstanding. Our current practice is vicious beyond imagination, once one thinks about it. If there are questions arising in the review of a project application, the supplicant will hear about them only after the peer panel has met and, often, only after a deferral that will have caused incalculable trauma. The straitened bandwidth of communication, the fantasies that too often underlie the judgments of the peer-review group without correction, these badly need reform with the help both of more human-scale procedures and of technologies like electronic mail and file maintenance. Our other gatekeeping systems, those of refereed publications and of faculty appointments, generally give more intimate contact with the submitter or more timely feedback and access to other options—other reviewers, or other gates. Meanwhile the current research project system gives disproportionate rewards to the grantsmen, those most skillful at verbiage for manipulating the system independent of the inherent scientific merit of their ideas. I am less sympathetic with the claim that these stresses in any way justify the incidents

of fraud and misrepresentation in science, each of which is so loudly advertised in the media. It may be, however, that the current system is attracting careerists into science impelled more by grantsy skills than their love for problem-solving for human benefit and for truth. We must be careful to return to these themes as our criteria of judgment.

The indirect effects of lengthened duration of awards would be equally valuable: it is more difficult for reviewers to slide into micromanaging projects of such duration. The focus of attention of the applicant would be redirected to basic goals and of the reviewers to the applicant's personal skills. The time given would allow for opportunistic exploration of unpredictable paths and for them to face the skepticism of the larger community.

The principal argument I have heard in defense of the short trolley ticket is the need to make room for young people. We must give careful attention to that. Yes, they may have difficulty competing with established investigators; they may have little but their project proposals to present as testimony of their skills. The perspective of trying to identify the most capable individuals does not, I would say, preclude the use of whatever testimony is relevant. We can of course give competitive points for youth, if that is our policy objective. We should keep in mind, however, that the principal use of funds in the hands of established investigators is precisely for the support of younger associates—certainly that has been my lifelong experience as student, as professor, and as administrator. I submit that the working professor is a better and highly interested judge of the qualifications of those associates than is a remote committee; undoubtedly, institutions could also enhance their local review procedures to assist in those evaluations. My own experience was also to have had the opportunity to earn my spurs and peer recognition through the work I did as a research fellow in Professor Tatum's laboratory. This system of apprenticeship has been institutionalized in the most consistent fashion in my present institution, The Rockefeller University, and there is abun-

dant historical evidence that it works very well. Finally, if we do really mean that the typical scientific career is going to be truncated in 7, even in 15 years, we really had better attend to all of the other insidious implications this has for the tenure system of the university.

The extreme, of lifelong tenure of research support, I do not advocate, even though that works reasonably successfully in systems like the British Medical Research Council and the intramural programs of government and of industry. There is some interval of recurrent accountability that must be optimal in balancing the stress of performance with the leisure and security for careful reflection; a seven-year cycle should be about right to keep track of the changing seasons of a scientific life. It is curious that many research managers who are sluggish to respond to my pleas are themselves permanently ensconced in their own bureaucratic niches. I don't advocate that they be put on a two-year leash to prove their performance—that would compound the disaster of short-run bottom-line accountability: a theme whose consequences for our industrial economy have been all too evident and certainly contributed to...Black Monday. But I hope they will be less insouciant about "keeping people on the trolley car" for an average total period that should be a single episode.

These cries in the wilderness have not gone utterly unheeded. The directors in our audience can give you details of their agencies' recent initiatives with experienced investigator awards and with lengthening the terms of grants and other simplifications of their procedures.

Program managers should also be allowed more flexibility to keep expiring grants "alive" for intervals long enough to allow the threshing out of misunderstanding or of other occasional but apparent failures of objective peer review. That flexibility is itself an administrative burden, but it will be more tolerable against the background of seven-year than of two-year awards. Finally, as a university administrator I would frequently have won the bet, if I could make it, of

placing funds on a project on the gamble that it would be eventually renewed. Some means should be found for the retrospective reimbursement of such gambles when they are in fact legitimated by later reexamination. That is not merely fair-dealing; it also enables and encourages insightful management on the part of the university administration. Of course I have to make such gambles anyhow, but with short shrift for explicit reimbursement when I am right, intended to offset (the hypothetical case) when I am too optimistic. In fact, I can't remember the last time an investigator that I grubstaked didn't "get back on the trolley car"; the net effect is almost always just a lot of lost energy (and a dwindling of reserves).

Industrial contractors have access to risk capital, invested as against expectation of future profit, that is denied to not-for-profit institutions. The measures just suggested are in the spirit of many others that would reward institutional as well as personal skills in the management of creative science. The present system of grant funding not only makes no provision for that risk capital, it subjects what there is to constant attrition: unilateral flows from cost sharing, incomplete indirect cost recovery, infrastructural costs, the whole system of faculty compensation that exchanges modest salaries for lifelong job security. Not allowable as "indirect costs" are the career-supporting burdens, attending to the gestation and early nurture of academic investigators, start-up and tide-over expenses, even the terminal care that is part of the system's social contract.

We should jealously guard the pluralism in government support of science that is one of our greatest safeguards against monumental and monolithic error. One agency can experiment and offer cues to improving the system for others.

4. *We must share responsibility.*

The entire burden of renovation of the research environment should not and cannot rest solely on federal reform. There is much to attend to in our own houses.

Unhappily, too many institutions have been socialized to accommodate to their dependence on the existing system and with reduced power their directors have abdicated what leadership they might still exercise in the management of research. Such a sweeping generalization is of course subject to notable but rare exceptions.

All too often the department has become the largest unit that sustains much intellectual and academic cooperation. Students funded from one project can spend some time in another lab in the same department; there is no comparable facility across broader reaches of the university. Above all the project funding system has further bolstered the imperatives of specialization; many able professors have little experience and little culture beyond the domain of their discipline [projects]. The project system further preempts the loyalties that might be directed to one's colleagues and one's institution in favor of the nationally centralized fount. In that milieu there is little incentive or latitude for leadership of any breadth even within science. Both these structural impediments, and the rarity of the appropriate talent, make it ever more difficult to install department chairs, deans, or provosts who are cognitively engaged with the content of the work they are called upon to administer. We are grateful when their political and human relations skills sustain some quiet among warring factions. Presidents, as Steve Muller and Jim March have lamented, are no longer expected to do more than raise money and empty the garbage can. Nor are faculty likely to be responsive, when their main task is to get their grants renewed. In consequence of these (and other) factors, many able scientists will properly refuse to involve themselves in formal administrative responsibilities: chairs, deanships, and other executive positions are going begging or are being filled by people with requisite high talents other than academic. It does not follow that scholarly attainment is a sufficient qualification for a managerial role; but without it the executive is ill equipped to make his own judgment of the merits of his colleagues' work, and he must struggle to sustain their

esteem and his or her authority. This depreciation of leadership is part of a vicious cycle of anarchy and its associated ills of splintering what ought to be a community of scholars. We all share responsibility for the exertions needed to restore that community, one that includes the teachers, the researchers, and the administrators.

5. *Some thoughts on "big science."*

Biology, until now, has rarely faced the need for megatechnologies to answer its primary scientific objectives. The human genome DNA-sequencing proposal does loom as a new way of doing business. This is a structure of formidable complexity: three billion nucleotide pairs of DNA, a full two meters of double helix if unraveled from a single cell. This corresponds to about 100,000 gene products that will have to be accounted for. The ultimate reductionism would be to build an analytical factory that could complete the reading of all three billion units as one technical exercise. A price tag of a few billion dollars is cited, perhaps less if there is prior investment in new technology to automate the task. Is it worth the cost? Undoubtedly! Is it the wisest use of that level of expenditure? I have very grave doubts! Part of my reservations have to do with the style of research it encourages, part with a misunderstanding about what we need to learn in "mapping the genome." We have by now profound information concerning a score or so of human proteins; each of them is at least a life's work. At a modest \$10 MM each, that would amount to a trillion dollars for the full set, and obviously we must make discriminating selections of targets before committing to the task. About 100 human proteins are now discernible as agents of important biological activity; that number will soon grow to perhaps 1,000. These should be the priority list for further inquiry. It will be far more important and more feasible to learn in depth about that percentile of the human genome than to have an exhaustive listing of a sequence of three billion nucleotides. For these, we will look

in detail into regulation, three-dimensional structure, genetic variability within and between species, physiological interrelationships, and therapeutic applications. To pursue such enquiries will take much more than the engineering mentality that would apply a single methodology for a single sweep. It will need a sense of the organism and a focused expertise on, even fascination for, the parts under scrutiny. This megaproposal does behoove us to sharpen a distinction between exploratory and exploitative phases of scientific development. Exploratory research engenders revolutionary breakthroughs with new perspectives; the agenda for exploitative science then becomes fairly obvious. For the latter, exquisite technical skills are to be recruited, but not too much imagination. Such projects can then be fairly readily judged by objective reviewers. There is little likelihood of plans being disrupted by totally unexpected discoveries—though this may happen even in the best regulated laboratory. Precisely because the DNA-sequence paradigm is so central to modern biology, it does set the agenda for almost all of the foreseeable, the plannable research at least of the next couple of decades. My fear is that it may also submerge new revolutions, not unlike the ones that initiated us into this phase of the history of biology.

Other sciences face very different challenges. Without large telescopes, accelerators, spacecraft, important regimes of the physical universe remain simply inaccessible to us. We have had good experiences in national facilities to provide these capabilities to a broad national community. There remain serious questions how to relate them to the life of the university. Much concern has been expressed that existing departmental structures frustrate broader and more innovative interests—and I have had my own experience of that. Genetics was certainly a stepchild at medical schools at the start of my career, and biochemistry not long before that. But I question whether larger "centers," if brought in top-down, won't aggravate the problem. By their allegiance to external sponsors, they will be even less ac-

countable to, and communicative with, their colleagues on their own campus. At the same time they will make inevitable calls on general resources that will weaken the university's flexibility in responding to other contingencies. We can answer these concerns (a) with appropriate sensitivity in the style of administration of these centers, and (b) by stronger internal leadership to contravene the splintering of the campus community into walled enclaves. Otherwise, we may again find that today's "new" centers are tomorrow's entrenched resistance to everchanging horizons.

Another challenge to introspection is whether we are doing all we can to accelerate "technology transfer" from academia to industry—a point of special sensitivity in the midst of today's anxieties about economic competitiveness. No one who knows my own personal history will accuse me of indifference to that issue. I will recall an anecdote about my professor, Edward L. Tatum, who completed his PhD in bacteriology at Wisconsin just 50 years ago and was facing a decision where to work. He was urged to

take a position at Iowa, to look into the then "hot" field of the microbiology of butter, one of manifest practical importance. Instead he went to Stanford, to work with G.W. Beadle on the eye pigments in fruit flies. That became translated within four years into their Nobel Prize winning work on the biochemical genetics of *Neurospora*, indubitably one of the principal foundations of today's biotechnology. It would have been tragic were any industry to have had a veto in deciding what would truly be of greatest industrial consequence. My own experience has been consistent with that theme, that the universities accept the difficult charge of leadership in pointing out where tomorrow's industries will find their greatest opportunities, many of them in the hands of corporations that will need new birth certificates—and so will not yet be at hand as the visible contemporary partners at the time the research is conceived.

The wisdom to oversee these complex technical relationships is still another challenge to the academic leadership of the future. Good luck.

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